

Remarks

Claims 1-13 are pending in the present application. Claims 1-13 have been rejected. By the present amendment, claims 1 and 12 are amended, and claim 13 is canceled.

***Rejections Pursuant to 35 U.S.C. §112, First Paragraph***

In the Office Action, claims 1-11 were rejected under 35 U.S.C. §112, ¶1, as based on a disclosure which is not enabling. In support of that rejection, the Examiner asserted that claims 1-11 recite a method for detecting an analyte but positively recite only a single step of adding a reagent to the sample, and that the specification fails to enable how such single step would result in detection of an analyte.

Claim 1 has been amended herein and recites a method for detecting an analyte by a redox reaction and a fluorimetric determination, comprising contacting a sample containing the analyte with a detection reagent which contains a compound of the general formula (I) as a fluorimetric redox indicator . . . irradiating the sample with excitation light of a predetermined wavelength; and detecting the presence of the analyte based on the fluorescence emission light emitted by the sample. Support for this amendment appears in ¶ [0016] and, therefore, no new matter has been added.

Claims 2-11 contain all of the limitations of claim 1, from which they depend. In view of the present amendment, applicants submit that the present application is in compliance with the statute and respectfully request that the rejection be withdrawn.

Also in the Office Action, claims 1-13 were rejected under §112, ¶1, as failing to comply with the enablement requirement. In support of that rejection, the Examiner asserted that the specification fails to teach how to make the claimed reagent.

With reference to ¶ [0003] of the specification, fluorometric determination procedures were generally known in the art at the time the invention was made.

Further, ¶¶ [0010 - 0011] of the specification describes the detection reagent, which contains a compound of the general formula (I) as a fluorimetric redox indicator. Moreover, ¶¶ [0012 – 0014] of the specification describe the manufacture of detection reagents in detail.

The disclosure was also objected to because the term NBD-amine is not adequately defined. Paragraph [0009] is amended herein, wherein “NBD” is defined as -- 7-Nitro-benz-2,1,3-oxadiazol --. No new matter has been added.

The corresponding NBD chloride is known as a fluorescent detection reagent for analytes, e.g., amines (c.f., excerpt from [www.roempp.com](http://www.roempp.com), enclosed herewith as Exhibit A). The implementation of the NBD chloride with amines leads to NBD amines (derivatised NBD with amines or substituted amines at position 4; see Journal für praktische Chemie, Vol. 326 (1984), pages 385-400). The composition shown in Fig. 1 of the present application is the N-oxide of the N,N-Di(hydroxyethyl)-NBD amine.

In view of these remarks, applicants submit that the present application is in compliance with the statute and respectfully request that the rejection be withdrawn.

### ***Rejections Pursuant to 35 U.S.C. §112, Second Paragraph***

Also in the Office Action, claims 1-13 were rejected under U.S.C. §112, ¶2 as being indefinite, i.e., the hand-drawn molecular structure is illegible.

Claims 1 and 12 are amended herein, wherein the hand-drawn compound of the general formula (I) is replaced with an equivalent computer generated image. No new matter has been added. Applicants submit that the claims currently pending are in compliance with the statute and respectfully request that the rejection be withdrawn.

***Rejections Pursuant to 35 U.S.C. §102***

Also in the Office Action, claims 12-13 were rejected under 35 U.S.C. §102(b) as being anticipated by Ghosh et al. (1968), in particular, Table 1.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Claim 13 is canceled herein, and its subject matter has been incorporated into claim 12, which now recites "[a] reagent for detecting an analyte by a redox reaction and a fluorimetric determination, comprising a compound of the general formula (I) . . . a first component selected from enzymes, coenzymes, auxiliary substances, buffers and mediators; and at least one further component selected from enzymes, coenzymes and a mediator." Support for this amendment appears in the claims as originally filed. Accordingly, no new matter has been added.

Ghosh et al., in contrast, teach benzo-2,1,3-oxadiazoles (benzofurazans) and their N-oxides (benzofuroxans) for use as anti-leukemic and immunosuppressive drugs. They do not teach or suggest a detection reagent, nor the particular reagent recited in amended claim 12. Ghosh et al. therefore cannot be relied upon in support of the instant rejection. Accordingly, applicants respectfully request that the rejection be withdrawn.

***Rejections Pursuant to 35 U.S.C. §103***

Also in the Office Action, claims 1-11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hoenes (U.S. Pat. No. 5,334,508) in view of Ghosh et al. (1968). The Examiner asserted in support of the instant rejection that although Hoenes differs from the instant claims in that the R1 and R2 substituents appear to be nominally different, Hoenes teaches the general utility of benzfuroxane derivatives, and Ghosh et al. disclose benzfuroxane derivatives that are the same as the compounds presently claimed. The Examiner further asserted it would have been obvious to one of

ordinary skill in the art to modify the method of Hoenes by selecting any known and available compound within the disclosed genus of benzfuroxane derivatives, including those listed and enabled by Ghosh et al.

The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. For the following reasons, applicants submit that the Examiner has not met this burden and respectfully request that the rejection be withdrawn.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. MPEP 2143 (*citing In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

In contrast to claim 1, as amended herein, Hoenes do not teach or suggest a method for detecting an analyte by a redox reaction and a fluorimetric determination comprising contacting a sample containing the analyte with a detection reagent which contains a compound of the general formula (I) as a fluorimetric redox indicator: . . . irradiating the sample with excitation light of a predetermined wavelength; and detecting the presence of the analyte based on the fluorescence emission light emitted by the sample. Compounds according to at least one embodiment of the present invention show a high fluorescence together with a good activation with blue, strong-light LEDs

(see ¶¶ [0007] and [0009]). Hoenes, in contrast, deals with colormetric detection systems – it does not teach or suggest fluorimetric assays, which are substantially different. In a colormetric assay, a change in color in the reaction mixture is determined. A fluorimetric assay, however, employs excitation of the fluorescent reagent with a specific wavelength and the detection of the fluorescent emission at a different wavelength. Hoenes does not teach or suggest fluorescent properties of benzforoxane derivatives. Moreover, Ghosh et al. do not fulfill the deficiencies of Hoenes, as Ghosh et al. merely teach therapeutic applications of benzfuroxane.

For these reasons, neither Hoenes nor Ghosh et al. can be relied upon in support of the present rejection. These references, either alone or in combination, do not teach or suggest the subject matter of claim 1, nor is there any suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Claims 2-11 contain all of the limitations of the base claim from which they depend. Applicants submit that the Examiner has not presented a *prima facie* case of obviousness and respectfully request that the rejection be withdrawn.

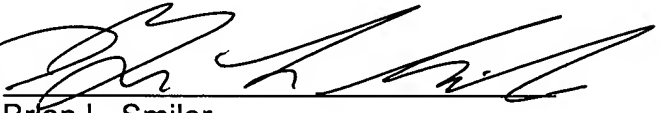
Applicants note the remaining prior art made of record in the Office Action. As that additional art is not applied by the Examiner against the claims of this application, the applicants are not providing any comments concerning the same at this time.

Conclusion

Applicants have filed a complete response to the outstanding Office Action and respectfully submit that, in view of the above amendments and remarks, the application is in condition for allowance. The Examiner is encouraged to contact the undersigned to resolve efficiently any formal matters or to discuss any aspects of the application or of this response. Otherwise, early notification of allowable subject matter is respectfully solicited.

Respectfully submitted,

ROCHE DIAGNOSTICS OPERATIONS, INC.

By   
Brian L. Smiler  
Reg. No. 46,458

9115 Hague Rd., Bldg. D  
Indianapolis, IN 46250-0457  
Telephone No.: (317) 521-3295  
Facsimile No.: (317) 521-2883  
E-mail: brian.smiler@roche.com  
BLS/